indicate that the difference must be "statistically significant," the new language finding support on page 4, line 28. It is believed that this term is recognized in the art as being a difference beyond experimental error. The Examiner is respectfully requested to withdraw these rejections.

Applicants' attorney thanks the Examiner for entering the amendments and providing an action on the merits. The Office Action will now be considered *seriatim*.

Paragraph 2 is noted.

Paragraph 3 is traversed. After citing the definition of the cells, which are used in the subject claimed invention, the phrase which defines the nature of the cells, namely "having enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells" is eliminated from consideration. Regardless of the mutation, the cells must fulfill the requirement of having enhanced potentiation. To what "unpredictable effects" is the Examiner referring? The effect of the mutation must be as indicated above and whether it is an excision, insertion, transversion or other mutation in the regulatory region or the gene, so long as it has the defined effect, it comes within the scope of the claims. The fact is that the cited art supports applicants' position. Whether such reference to Parent is properly of record may be left to a further day, as the reference is subsequent to the filing of the subject application. Nevertheless, the reference supports the evidence presented in the subject application by affirming that LTP response in mutant PS1 transgenic mice is higher. "...we found that in transgenic mice expressing the FAD-linked A246E variant, the amplitude of LTP expression is markedly elevated relative to mice expressing wild-type PS1. " These cells fulfill the requirement of enhanced potentiation and it is the effect of a drug on the enhanced potentiation that is the subject matter of the claimed invention. Whether under the conditions of the Parent assay and the subject assay, there were differences in the observed fEPSP, is not relevant, where both the subject investigators and the published investigators establish that there is a difference in the LTP, which difference is shown by the subject inventors to be a basis for screening for drugs.

It is submitted in light of the subsequent remarks concerning the unpredictability of *in vitro* screening, that the Examiner and applicants' attorney have a different view of what screening intends. First, it should be mentioned that under the guidelines, a screening methodology acceptable to the field is acceptable to the PTO. Secondly, a screening methodology is not a guarantee that a compound will be a successful drug. Its primary intent is to exclude compounds that do not have the relevant activity. It is the beginning, not the end, of the process of bringing a drug to the marketplace. As such, it has utility in avoiding further testing of compounds, which are not likely to be useful for the intended purpose. The subject invention provides a useful tool in the development of drugs for the treatment of Alzheimer's Disease. As such, it fulfills the statutory requirement of utility.

The rejection further indicates that the term "treatment" is too indefinite. The claims do not require that the compounds be used for treatment, but rather that the compounds be candidates for treatment of AD. As already indicated, the subject invention serves to narrow the field, which is believed to be a recognized utility for patentability. It is submitted that the

utility of the drug is being confounded with the utility of the method for screening for drugs. All that is required for screening is that there is a reasonable relationship between a positive result and activity for the indication for which the compound is being tested.

In conclusion, the rejection ignores the guidelines for what is acceptable for utility for a candidate drug. Much less should be required where the claimed invention is for a screening method for narrowing the field of candidate compounds. There is a rational nexus between the subject method and utility for a compound as a candidate for the treatment of AD. The subject method measures the restoration of potentiation as a result of tetanic stimulus toward a wild-type level. Under the appropriate guidelines, this should be sufficient, particularly where the inventors are world-renowned experts in the field.

For all of the above reasons, the Examiner is respectfully requested to withdraw these rejections under 35 USC §112 first paragraph.

Paragraphs 4 and 5 have already been addressed.

Paragraph 6 is respectfully traversed. It is respectfully submitted that the Examiner is misinterpreting the terms of the claim. By no stretch of the imagination can one consider an antibody for a neural protein a drug, no less a candidate drug. There is no indication in the reference that the antibodies to amyloid protein have any activity of a drug or are being considered as a candidate for such use. The Examiner is respectfully requested to withdraw the rejection.

In view of the above amendments and remarks, the application is considered in good and proper form for allowance and the Examiner is respectfully requested to withdraw the rejections and pass this application to issue. If the Examiner believes that a telephonic interview would expedite the prosecution of the application, the Examiner is authorized to call the undersigned collect at 650 328-4400.

Respectfully submitted,

Dated: 11/17/99

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